A Prebiotic Surface Catalyzed Photochemically Activated Synthesis of 5,6-Dimethylbenzimidazole of Vitamin B12

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Abstract: - Alkynes such as but-2-ynimine and but-2-yne nitrile form weak charge-transfer complexes with catalysts such as Mg.porphin centered on the Mg^{++} ion and a pyrrole nitrogen. With two bonded adducts electromagnetic excitation produces a high energy bicyclic complex. Further reaction with molecular hydrogen produces a bound di-nitrilo complex and then a di-imino complex that separates from the catalyst. Reaction with formaldehyde produces the rare base 5,6-dimethylbenzimidazole found in Vitamin B12.
The reactions have been shown to be feasible from the overall enthalpy changes in the ZKE approximation at the HF and MP2 /6-31G* level.

Key-Words: 5,6-dimethylbenzimidazole ,Mg.porphin , but-2-ynimine, but-2-yne nitrile, cyanogen.

1 Introduction

5,6-Dimethyl-1*H*-benzimidazole [1], 5,6-dimethylbenzimidazole, in which the nitrogen atoms are equivalent [2] occurs as an axial ligand of adenosylcobalamin (coenzyme B12) a structurally complex cobalt-containing cyclic tetrapyrrolidine/ pyrroline [3] synthesized by diverse groups of prokaryotes. These bacteria synthesize 5,6-dimethylbenzimidazole (DMB) from riboflavin-5'-phosphate (FMN) [4] where the conversion is oxygen-dependent with the C-1 carbon of the ribose moiety of FMN becoming the C-2 carbon of DMB. This synthesis is similar to organic syntheses where the nonenzymatic spontaneous synthesis of DMB occurs from 4,5-dimethylphenylenediamine and ribose-5-phosphate. The o-phenylenediamines may also use acid, acid anhydride, aldehyde, or diketones to close the imidazole ring [5,6]

From a prebiotic perspective [7] it is desirable if the reactant molecules formed spontaneously from a supposed prebiotic atmosphere to be inevitably present. It has often been held that the atmosphere of the Earth was originally mildly reducing [8,9] implying the presence of concentrations of carbon monoxide, ammonia, water and hydrogen. It is also supposed that alkynes such as acetylene [10,11] were present as found on Titan, a moon of Saturn. It has also been demonstrated that porphin may act as a catalyst for the formation of sugars [12] and polyenes [13].

This paper proposes a model for the surface catalytic photochemically activated formation of dimethylbenzimidazole from the gases, propyne, hydrogen cyanide and hydrogen with the surface catalyst, magnesium porphin . Experimental gaseous mixture subjected to discharge have been shown to produce biomolecules [14].

2 Problem Formulation

The computations tabulated in this paper used the GAUSSIAN98 [15] commercial package. The standard calculations at the HF and MP2 levels including zero-point energy corrections (HF) [16], together with scaling [17], using the same basis set, 6-31G*, are as previously published [7]. Enthalpy changes at the MP2 level not including scaled zero point energies are designated as $\Delta H_{(MP2)}$. All ZPE energies are HF. The charge transfer complexes are less stable when calculated at the Hartree Fock level [16].

If the combined energy of the products is less than the combined energy of the reactants it may show that the reaction is also likely to be spontaneous at higher temperatures. This paper uses the atomic unit of energy, the hartree [15].

$1h = 627.5095\ kcal.mol^{-1}$.
$1h = 4.3597482 \times 10^{-18}\ J$

3 Problem Solution

3.1 Total energies (hartrees)

Molecules that are present interstitially and in planets [18,19] are here taken to be the initial reactant molecules: propyne, and hydrogen cyanide, where the formation of the but-2-yne nitrile and but-2-ynimine (cis) may be produced by atmospheric free radical or ionic reactions [18].

$CH_3\text{-}C \equiv C\text{-}H + H\text{-}CN \rightarrow CH_3\text{-}C \equiv C\text{-}CN + H_2$ [1]

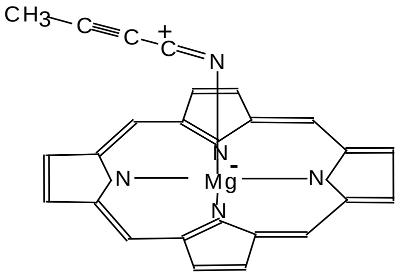
$\Delta H = -0.00816$ h

$CH_3\text{-}C \equiv C\text{-}CN + H_2 \rightarrow CH_3\text{-}C \equiv C\text{-}CH{=}NH$ (cis) [2]

$\Delta H = 0.00444$ h

The catalyst Mg.porphin, readily forms adducts with a variety of molecules [20]. It forms a weak charge transfer complex with but-2-yne nitrile where the ligand is positively charged (0.09) and the porphin has a negative charge, as shown,

Mg.porphin + $N \equiv C\text{-}C \equiv C\text{-}CH_3 \rightarrow$
(1)

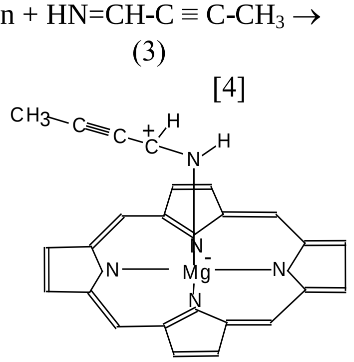


Mg.1,N-but-2-yn-nitrilo.porphin (2) [3]

$\Delta H = -0.02403$ h

The catalyst also forms a weak charge transfer complex with but-2-ynimine where the ligand is positively charged (0.07) and the porphin has a negative charge, as shown,

Mg.porphin + $HN{=}CH\text{-}C \equiv C\text{-}CH_3 \rightarrow$
(3)
[4]



Mg.1,N-but-2-yn-imino.porphin (cis) (4)

$\Delta H = -0.04014$ h

Adducts may also be centered on the pyrrole nitrogen atoms [12,13].

Both of these adduct complexes may be used in the following synthesis which only depicts the Mg.1,N-but-2-yn-nitrilo.porphin.

The data for the total energies and zero point energies for the HF and MP2/6-31G* equilibrium geometries for these molecules and others involved in the synthesis are given in Table.1.

Table 1

MP2 /6-31G* total energies and zero point energies (hartrees) for the respective equilibrium geometries

Molecule	MP2 hartree	ZPE (HF) hartree
but-2-yne nitrile (1)	-208.25777	0.05963
Mg.1,N-but-2-yn-nitrilo.porphin (2)	-1393.39992	0.34733
but-2-ynimine (3)	-209.41044	0.08479
Mg.1,N-but-2-yn-imino.porphin (cis) (4)	-1394.57494	0.37950
5,6-dimethylbenzimidazole (5)	-457.02185	0.18558
Mg.1,N-but-2-yn-nitrilo.porphin.N-but-2-yn-nitrilo (6)	-1601.65719	0.40870
Mg,1,N-but-2-yn-imino.porphin.N-but-2-yn-imino (7)	-1603.98839	0.45944
Mg.1, bicyclo[2,2,0] hex-1,3-dien-1,N,5,6-di-nitrilo.porphin (8)	-1601.43184	0.41169
Mg.1, 4,5-dimethyl-1,N2-di-nitrilo benzene.porphin (9)	-1602.77993	0.43971
Mg.1, 4,5-dimethyl-1,N2-di-imino benzene.porphin (10)	-1604.06103	0.46549
1,2-di-imino 4,5-dimethyl benzene (11)	-418.95758	0.17831
1-methanolimino-2-imino 4,5-dimethyl benzene. (12)	-533.14059	0.21377
5,6-dimethyl benzo-1,3-didehydro iminazolidine (13)	-456.97519	0.18492
Mg.porphin	-1185.12250	0.29262
propyne	-116.24181	0.06010
H-CN	-93.15894	0.01593
$CH_2{=}O$	-114.16775	0.02920
H_2	-1.14414	0.01059
OH^-	-75.51314	0.00885
H_2O	-76.19685	0.02298

3.2 The overall stoichiometry for the formation of 5,6-dimethylbenzimidazole.

Although Mg.porphin is here taken as the catalyst for the reaction, the overall stoichiometry for the synthesis of 5,6-dimethylbenzimidazole from but-2-yne nitrile and formaldehyde can be represented as follows,

$$2\ CH_3\text{-}C \equiv C\text{-}C \equiv N\ +\ 2H_2\ +\ CH_2 = O \rightarrow C_9H_{10}N_2\ +\ H_2O \qquad [5]$$

5,6-dimethylbenzimidazole (5)

$\Delta H = -0.21249$ h

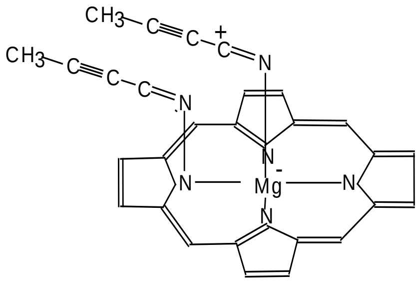
The enthalpy change is negative indicating that there may be energetically favourable routes to the formation of this molecule from these reactants.
The intermediates by which the stoichiometric reactions may have occurred are as follows:

3.3 The Formation of 5,6-dimethyl benzimidazole.

3.3.1. The formation of the Mg.1,N-but-2-yn-nitrilo.porphin.N-but-2-yn-nitrilo

Mg.porphin is a powerful catalyst able to form charge transfer complexes with a number of different kinds of molecules [20]. But-2-yne nitrile forms a weak charge transfer complex with the Mg ion of the catalyst Mg.porphin, and a weak van der Waals adduct centered on a pyrrole nitrogen atom. The charges on the two adducts are different. The first adduct carries a positive charge of 0.01 whilst the latter has a charge of 0.05 as shown,

$$\text{Mg.porphin} \quad +\quad 2\ CH_3\text{-}C \equiv C\text{-}C \equiv N \rightarrow$$



Mg.1,N-but-2-yn-nitrilo.porphin.N- but-2-yn-nitrilo (6) [6]

$\Delta H = -0.02198$ h

The analogous Mg,1,N-but-2-yn-imino.porphin.N-but-2-yn-imino (7) complex is also formed with a favourable enthalpy change,

$$2\ CH_3\text{-}C \equiv C\text{-}CH = NH + \text{Mg.porphin} \rightarrow \text{Mg,1,N-but-2-yn-imino.porphin.N-but-2-yn-imino (7)} \qquad [7]$$

$\Delta H = -0.04747$ h

Under the influence of electromagnetic radiation the Mg.1,N-but-2-yn-nitrilo.porphin.N- but-2-yn-nitrilo (6) is postulated to bond forming a high energy complex, as shown,
.
Mg.1,N-but-2-yn-nitrilo.porphin.N- but-2-yn-nitrilo (6) →

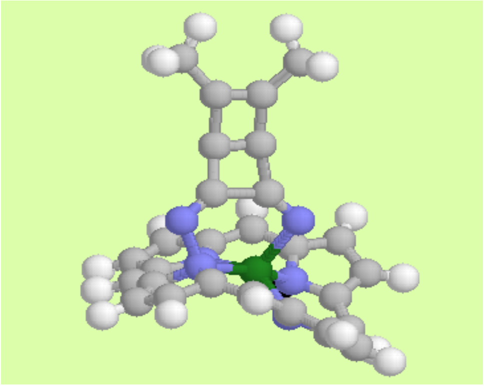


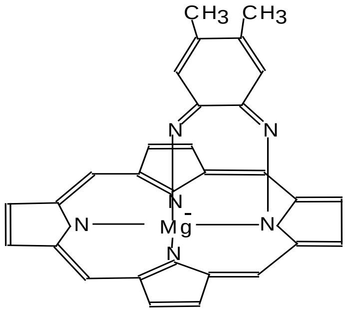
Fig.1. Mg.1, bicyclo[2,2,0] hex-1,3-dien-1,N,5,6-di-nitrilo.porphin. (8) [8]

$\Delta H = 0.22801$ h

As the enthalpy change is appreciable and positive it is postulated that this occurs by electromagnetic excitation where the first excitation of these very weak complexes requires about 0.21 h. The activation energy to form the complex was calculated as 0.205 h at HF accuracy, with the activation energy for the reverse reaction being 0.052 h.
The high energy di-adduct complex is then susceptible to hydrogenation with molecular hydrogen.

3.3.2. The formation of the Mg.1, 4,5-dimethyl-1,N2-di-nitrilo benzene.porphin

The Mg.1, bicyclo[2,2,0] hex-1,3-dien-1,N,5,6-di-nitrilo.porphin may react with molecular hydrogen with a spontaneous opening of the bicyclic ring structure, Mg.1, bicyclo[2,2,0] hex-1,3-dien-1,N,5,6-di-nitrilo.porphin + H_2 →



Mg.1, 4,5-dimethyl-1,N2-di-nitrilo benzene.porphin (9) [9]

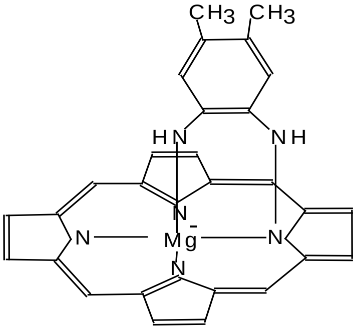
$\Delta H = -0.18843$ h

The activation energy was recorded as 0.090 h,with the reverse reaction having an activation energy of 0.304 h.

3.3.3. The formation of Mg.1, 4,5-dimethyl-1,N2-di-imino benzene.porphin

The Mg.1, 4,5-dimethyl-1,N2-di-nitrilo benzene.porphin may react further with molecular hydrogen,

Mg.1, 4,5-dimethyl-1,N2-di-nitrilo benzene.porphin + H_2 →



Mg.1, 4,5-dimethyl-1,N2-di-imino benzene.porphin (10) [10]

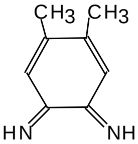
$\Delta H = -0.60537$ h

The activation energy was recorded for this hydrogen addition as 0.086 h, with the reverse reaction requiring 0.251 h.

3.3.4. The disscociation of the 1,2-diamino 3-4-dimethyl benzene from the Mg.porphin catalyst.

The complex with the catalyst is calculated to spontaneously separate with a favourable energy change,

Mg.1, 4,5-dimethyl-1,N2-di-imino benzene.porphin → Mg.porphin +



1,2-di-imino 4,5-dimethyl benzene (11) [11]

$\Delta H = -0.01421$ h

3.3.5. The reaction of 1,2-diamino 4,5-dimethyl benzene with formaldehyde.

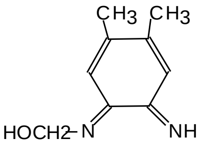
Formaldehyde is expected to be present in an original atmosphere containing carbon monoxide if it was mildly reducing,

$CO + H_2 \rightarrow H_2C{=}O$ [12]

$\Delta H = 0.00923$ h

The reaction of a base with an aldehyde is usually a classic acid –base catalyst reaction as depicted here,

1,2-di-imino 4,5-dimethyl benzene + $H_2C{=}O$ →



1-methanolimino-2-imino 4,5-dimethyl benzene. (12) [13]

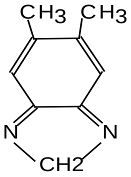
$\Delta H = -0.00970$ h

If the formaldehyde molecule is protonated in the acid –base environment then no activation energy was calculated for the addition.

3.3.6 The formation of 5,6-dimethyl benzo-1,3-didehydro iminazolidine

1-methanolimino-2-imino 4,5-dimethyl benzene. (12) may cyclise under acid base conditions in a favourable reaction,

1-methanolimino-2-imino 4,5-dimethyl benzene. (12) → H_2O +



5,6-dimethyl benzo-1,3-didehydro iminazolidine (13) [14]

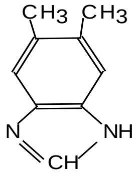
$\Delta H = -0.03667$ h

If the methanolimino group is protonated then an activation energy to form the C-N bond was calculated as 0.073 h.

3.3.7. The formation of 5,6-dimethyl benzimidazole.

The 5,6-dimethyl benzo-1,3-didehydro iminazolidine may isomerize in an an energetically favourable reaction,

5,6-dimethyl benzo-1,3-didehydro iminazolidine →



5,6-dimethyl benzimidazole (5). [15]

$\Delta H = -0.04608$ h

Whilst the above synthesis appears to be viable it seems unlikely that only one synthetic method was available. Here, a second postulated synthesis is described where the initial reactants would be the same, namely, propyne, hydrogen cyanide and hydrogen. However, it relies on the formation of cyanogen gas.

3.4 The formation of 1,2-di-imino 4,5-dimethyl benzene

3.4.1. The overall stoichiometry for the formation of 1,2-di-imino 4,5-dimethyl benzene

Cyanogen may be formed to some extent from the disproportionation of hydrogen cyanide by free radical reactions in the atmosphere, as,

$2\ H\text{-}C \equiv N \rightarrow (CN)_2 + H_2$ [16]

$\Delta H = 0.00993$ h

$N \equiv C - C \equiv N + 2\ CH_3\text{-}C \equiv C\text{-}H + H_2 \rightarrow C_8H_{10}N_2$
1,2-di-imino 4,5-dimethyl benzene (11) [17]

$\Delta H = -0.14620$ h

The data for the total energies and zero point energies for the HF and MP2/6-31G* equilibrium geometries for these molecules and others involved in this synthesis are given in Table.2.

Table 2
MP2 /6-31G* total energies and zero point energies (hartrees) for the respective equilibrium geometries

Molecule	MP2 hartree	ZPE (HF) hartree
cyanogen (14)	-185.57513	0.01820
cyanogen$^+$ (15)	-185.41009	0.03022
propyne$^-$ (16)	-115.59388	0.04653
1-imino but-2-yne cyanide (17)	-301.41745	0.08414
4,5-di-imino-2,6-octadiyne (18)	-417.67005	0.14990
1,2-di-imino-3,6-didehydro 3,4-dimethyl benzene. (19)	-417.58322	0.14955
CO	-113.02122	0.00556

3.4.2 The formation of 1-imino-but-2-yne cyanide.

Cyanogen gas may react with propyne under conditions of acid/base catalysis, provided the cyanogen is first protonated as,

$N \equiv C - C \equiv N + H^+ \rightarrow N \equiv C - C \equiv NH^+$
(14) (15) [18]

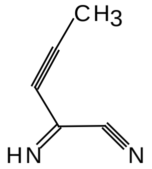
$\Delta H = -0.24188$ h

and the propyne has also become ionized in the mildly alkaline environment as,

$CH_3\text{-}C \equiv C\text{-}H + OH^- \rightarrow CH_3\text{-}C \equiv C\text{-} + H_2O$
(16) [19]

$\Delta H = -0.02329$ h

$N \equiv C - C \equiv N + CH_3\text{-}C \equiv C\text{-}H \rightarrow$



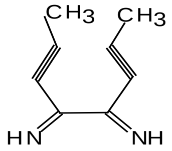
1-imino but-2-yne cyanide (17) [20]

$\Delta H = -0.01293$ h

3.4.3 The formation of 4,5-di-imino-2,6-octadiyne.

An analogous reaction with another propyne anion is also favorable,

1-imino but-2-yne cyanide + $CH_3\text{-}C \equiv C\text{-}H \rightarrow$



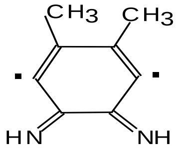
4,5-di-imino-2,6-octadiyne (18) [21]

$\Delta H = -0.00575$ h

3.4.4 The formation of 1,2-di-imino-3,6-didehydro 3,4-dimethyl benzene.

Ring closure gives the 1,2-di-imino-3,6-didehydro 3,4-dimethyl benzene.

4,5-di-imino-2,6-octadiyne →



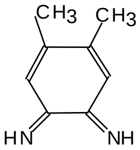
1,2-di-imino-3,6-didehydro 3,4-dimethyl benzene. (19) [22]

$\Delta H = 0.08652$ h

The activation energy to close the ring was 0.128 h and 0.019 h to dissociate the ring at the HF level of accuracy

3.4.5 The formation of 1,2-di-imino 3-4-dimethyl benzene

1,2-di-imino-3,6-didehydro 3,4-dimethyl benzene. + H_2 →



1,2-di-imino 4,5-dimethyl benzene (11) [23]

$\Delta H = -0.21404$ h

The activation energy for the addition was calculated by straddling the hydrogen molecule between the unsaturated carbons. The activation for the addition was found to be 0.070 h and 0.325 for the reverse reaction.

4. Conclusion

This postulated synthesis closely follows that suggested for the prebiotic synthesis of riboflavin [23] where propyne is the source of the dimethyl groups in both cases. The derivative propyne cyanide, is the reactant here, and the suggested monomer for the prebiotic synthesis of the four cyclic pyrrolidine rings of corrin in Vitamin B12 [24,25]. The formation of dimethyl di-imino benzene suggests that it may have been formed on the surface of the corrin and reacted directly with the ribose forming there [26] similar to its biochemical conversion from riboflavin [4].

Further work at a higher accuracy may alter the values given here

5 Acknowledgements

Appreciation is expressed for the advice and support given to this project by Professor Curt Wentrup of the University of Queensland.

Appreciation is also expressed to the National Computing Infrastructure facility supported by the Australian Government (grant NCI-MAS g01) and QCIF, and the assistance of Mr.D.Green, H.Hartig, M.Hankel and M.Nicholls.

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